[ORIGINAL RESEARCH]

# Severely Mood-disordered Youth Respond Less Well to Treatment in a Community Clinic than Youth with Bipolar Disorder

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## ABSTRACT

**Objective:** A tremendous increase in the diagnosis of bipolar disorder in pediatrics raises questions about current diagnostic practices. Even though researchers are providing initial follow-up data about rigorously diagnosed bipolar youth versus youth with severe nonbipolar mood symptomatology, not much is known about these different patient groups in the community. This study used standardized assessment tools to evaluate if meaningful differences emerge between different mood disorder types in children.

**Design:** The Mini International Neuropsychiatric Interview and the Child/Adolescent Symptom Inventory were used to classify patients as having bipolar disorder or mood disorder not otherwise specified (NOS) according to criteria set forth by the National Institute of Mental Health. A retrospective chart review followed back the treatment for eight months.

**Setting:** A community mental health clinic.

**Participants:** 41 pediatric patients between six and 18 years old.

**Measurements:** Global Assessment of Functioning scale and

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**KEY WORDS:** pediatric, bipolar disorder, mood disorder NOS, diagnosis, treatment response

Clinical Global Impression scales were compared pre- and post-treatment.

**Results:** Patients with bipolar disorder improved significantly more than mood disorder NOS patients, despite similar levels of care. Meaningful differences in diagnostic and treatment variables were apparent at baseline and at endpoint.

**Conclusion:** Standardized assessments in community clinics are feasible and lead to the identification of meaningful differences between "similar" patient groups. Improving diagnostic practices across different psychiatric settings appears paramount.

## INTRODUCTION

Recently, there has been a significant increase in the diagnosis of bipolar disorder in youth.[1] Within the last decade, this diagnosis in children and adolescents has more than doubled.[2] There are a number of possibilities explaining this dramatic increase. Perhaps an unknown biological variable, causing an actual increase of bipolarity in the pediatric population, exists. Perhaps this change is due to a more comprehensive understanding of the disorder. Or, perhaps the surge of diagnoses is due to a combination of diagnostic confusion and poor diagnostic practices.

Often determining which disorders plague a child can be challenging due to a variety of factors, including comorbidity (i.e., a series of disorders frequently occurring simultaneously, such as attention deficit hyperactive disorder [ADHD], oppositional defiant disorder, and bipolar disorder).[3] In community practices today, there seems to be a habit of categorizing a series of similar, yet fundamentally distinct, disorders under the heading of bipolar disorder.[4] However, with the advancements of psychiatry in the modern era, including new medications and new diagnostic classifications, it is more important than ever to differentiate between disorders. Conditions in youth can continue into adulthood with complicated symptoms; therefore, it is essential to diagnose properly from an early age. Furthermore, the imperfections of medications and their often serious side effects strengthen the desire to avoid intensive use if not critically necessary. Thus, on these two counts, the correct diagnosis and treatment is vital in psychiatric practice.

More specifically, in the case of pediatric bipolar disorder, it is crucial to distinguish between severely mood disordered youth and actual bipolar disordered youth. Data from the National Institute of Mental Health (NIMH) clearly delineate the importance of diagnostic differentiation between these two conditions. The data underscore this necessity by suggesting that severely mood disordered, but not bipolar disordered, youth may be significantly at risk for developing unipolar depression in adulthood, but not adult bipolar disorder.[5]

Leibenluft describes a series of four phenotypes of "bipolarity" in the pediatric population.[6] The phenotypes range from the *Diagnostic and Statistical Manual of Mental Disoders, Fourth Edition, Text Revision* (DSM-IV-TR) definition of bipolar disorder to severely mood disordered youth. These latter patients are characterized by hyper-arousal and severe irritability, but not by core manic symptoms of euphoria, grandiosity, decreased need for sleep, hypersexual behavior, and racing thoughts. Phenotype I matches both the symptomatic and duration criteria of the DSM-IV-TR for bipolar disorder. Phenotype II matches the symptomatic criteria but not the duration criteria. Phenotype III does not match the symptomatic criteria for mania or hypomania, but cycling is present with irritability as the predominant mood. And, finally, phenotype IV references youth without symptomatic criteria and without cycling, but with chronic severe irritability. Patients in the latter groups are considered to be severely mood disordered, yet not bipolar.

Often in clinical practice, all of the phenotypes are deduced to be bipolarity, though this certainly may not be the case, as evidenced by the NIMH study. Unfortunately, there is little data in community practice highlighting the differences between bipolar disorder and severely mood disordered pediatric patients. Therefore, this study is an initial pilot study to look at two samples, one with bipolar disorder and one with severe mood disordered symptomatology, to see if any meaningful differences emerge. In this paper, Leibenluft's phenotypes I and II will be referenced as pediatric bipolar disorder, while phenotypes III and IV will be referenced as mood disorder not otherwise specified (NOS).

## METHODS

A retrospective chart review included all patients, five to 18 years of age, who underwent a psychiatric evaluation between September 2004 and September 2007, and were diagnosed with bipolar disorder or mood disorder NOS. A psychiatric evaluation by a board-certified child and adolescent psychiatrist in this clinic includes the administration of the Mini International Neuropsychiatric Interview for Children and Adolescents[7] to the patient and the completion of the Child/Adolescent Symptom Inventory[8] by the parent. Patients were diagnosed with bipolar disorder I or II when they fulfilled full DSM-IV-TR criteria and with bipolar disorder NOS when they showed discrete episodes of core hypomanic/manic symptom clusters, such as euphoria, grandiosity, decreased need for sleep, hypersexual behavior, and racing thoughts, for at least four hours duration, at least once per week.[9] Patients were diagnosed with a mood disorder NOS when they showed a significant mood disturbance of severe irritability, cyclical or not, and did not have discrete episodes of core hypomanic/manic symptoms, even though they may have had

sporadic, isolated core hypomanic symptoms.[6] Figure 1 provides an example of a patient diagnosed with a bipolar disorder and a patient diagnosed with a mood disorder NOS.

Patients were included if they returned for at least one follow-up visit after the start of pharmacotherapy. In general, patients were started on pharmacotherapy immediately after the initial evaluation, were scheduled for a return visit one month later, and were subsequently seen for follow-up visits every two to three months. Follow-up visits included both patients and parents to review progress, side effects, mental status, and the medication regimen. As part of every follow-up visit, a Global Assessment of Functioning (GAF) score was determined. Data were documented in a standardized chart format.

Patients were treated with mood stabilizers/anti-aggression medications, most commonly aripiprazole.[10] The decision to treat with mood stabilizers was made with informed consent/assent of the parent and the patient.

The chart review included historical information obtained during the initial evaluation and "followed back" the treatment course until either the patient dropped out of treatment or until the last visit within the first year after the initial evaluation. As such, data were only obtained for a maximum of one year of treatment. Information extracted from the records included age at initial evaluation, gender, DSM-IV-TR diagnoses, including initial GAF, family history of bipolar disorder, number of prior psychiatric hospitalizations, highest level of care ever required (1=outpatient psychotherapy, 2=wraparound or family-based therapy, 3=partial hospitalization program, 4=residential care/hospitalization), previous number and type of medications used, risk factors for suicidality routinely collected in this clinic (e.g., past or present suicidal ideation, past or present suicidal behavior, family history of suicidal behavior, exposure to suicidal behavior, history of physical or sexual abuse, history of psychiatric hospitalization, and substance use), medications prescribed after the evaluation, changes made in the prescription, number of medications used during the treatment, and final GAF. A Clinical Global Impression-Improvement Score (CGI) was extracted from the report of the last treatment visit, compared to the initial evaluation.

Statistical comparisons were done with Student's t-test for continuous variables and Chi-square test for categorical variables. Tests were two-tailed and significance was put at the 0.05 level.

BIPOLAR DISORDER
The patient reports periods of feeling high and full of energy. He reports needing less sleep, feeling significantly irritable, talking too much, racing thoughts, distractibility and dangerous behavior. Other times, he reports low mood, feeling uninterested in normal activities, and ambivalence regarding spending time with friends and family. The patient reports that his mood will fluctuate and cycle about 2 to 3 times per week. High and low episodes last 2 to 3 days at a time.

MOOD DISORDER NOS
The patient is described as chronically irritable. Irritability leads to aggressive and violent behavior. Examples include biting his brother to the point of bleeding, and hitting and biting children in school. At times, the patient presents as somewhat overconfident such as "telling the school teacher how stupid she was". No significant hypomanic symptoms such as euphoria, decreased need for sleep, racing thoughts and pervasive grandiosity are reported. No significant depressed mood or anhedonia are reported.

**FIGURE 1.** Example of a patient diagnosed with a bipolar disorder and a patient diagnosed with a mood disorder NOS

**TABLE 1.** Baseline characteristics

| PATIENT CHARACTERISTICS | Mood Disorder NOS | Bipolar Disorder | *P* value |
|---|---|---|---|
| | *N*=22 | *N*=19 | |
| Age | 11.3±3.1 | 15.0±2.4 | 0.0002 |
| Gender (male) | 15 | 12 | >0.5 |
| Diagnoses (*n*) | 2.4±1.1 | 2.1±0.7 | 0.218 |
| ADHD present | 18 | 11 | >0.1 |
| + Family history | 14 | 11 | >0.5 |
| Risks (*n*) | 1.0±1.2 | 1.6±1.3 | 0.133 |
| Past inpatient | 9 | 10 | >0.5 |
| Past medications (*n*) | 2.7±2.7 | 3.7±3.2 | 0.309 |

+ Family history = for bipolar disorder; Risks = risks for suicidal behavior; Past inpatient = number of patients with psychiatric hospitalizations; Past medications = number of reported past psychiatric medication trials

## RESULTS

Twenty-two patients were identified as having been diagnosed with mood disorder NOS and 19 patients with bipolar disorder. Characteristics of both groups are listed in Table 1. Patients with bipolar disorder were about four years older, had more risk factors for suicidality (63% of patients with past suicidality versus 45%), more

**TABLE 2.** Treatment results

| TREATMENT | MOOD DISORDER NOS | BIPOLAR DISORDER | *P* VALUE |
|---|---|---|---|
| | *N*=22 | *N*=19 | |
| Follow-up (m) | 7.8±3.8 | 7.8±3.7 | 0.953 |
| Level of care | 2.0±1.3 | 2.1±1.3 | 0.718 |
| Medications (*n*) | 2.5±1.4 | 2.5±1.9 | 0.97 |
| GAF baseline | 45.0±5.1 | 46.6±5.0 | 0.326 |
| GAF endpoint | 50.3±8.4 | 56.9±8.0 | 0.014 |
| Change in GAF | 5.3±10.2 | 10.3±10.7 | 0.131 |
| CGI | 3.1±1.3 | 2.6±1.2 | 0.211 |

Level of care = highest level of care ever required (1=outpatient psychotherapy, 2=Family based therapy/wrap-around, 3=partial program, 4=residential care/hospitalization); medications = total number of medications used during this study.

**TABLE 3.** Medications to treat primary condition

| MEDICATION | MOOD DISORDER NOS | MOOD DISORDER NOS | BIPOLAR DISORDER | BIPOLAR DISORDER |
|---|---|---|---|---|
| | Initial (*n*) | Endpoint (*n*) | Initial (*n*) | Endpoint (*n*) |
| Aripiprazole | 13 | 13 | 13 | 9 |
| Risperidone | 6 | 3 | 0 | 1 |
| Quetiapine | 0 | 1 | 0 | 0 |
| Ziprasidone | 0 | 0 | 1 | 2 |
| Perphenazine | 1 | 0 | 0 | 0 |
| Lamotrigine | 1 | 1 | 2 | 5 |
| Divalproex | 0 | 0 | 2 | 3 |
| None | 1 | 3 | 1 | 0 |

inpatient hospitalizations (53% of patients vs. 41%), and had more past medication trials. Patients with mood disorder NOS had more ADHD diagnoses (82% vs. 58%), more overall diagnoses, and more family histories of bipolar disorder (64% vs. 58%). The only statistically significant difference between the two groups was in age.

After approximately eight months of follow-up, patients diagnosed with bipolar disorder improved significantly more as manifested by their endpoint GAF. Even though not statistically significant, their CGI and change in GAF were much better as well. Patients were treated with an average of 2.5 medications, while their highest level of care did not differ. Table 2 summarizes these findings. In Table 3, the medications to treat the primary disorder, initially and at endpoint, are listed. The overwhelming majority was treated with atypical antipsychotic monotherapy for the mood problems, although many were prescribed anti-ADHD medications as well (mood disorder NOS: seven treated with stimulants and seven with atomoxetine; bipolar disorder: two treated with stimulants and five with atomoxetine).

## DISCUSSION

The results of this study need to be interpreted in light of its limitations. Sample sizes were small, which more than likely reduced the statistical power to find significant differences. Treatment was uncontrolled and data were collected retrospectively. Adherence to treatment was unchecked. Many patients received concomitant psychosocial treatments.

On the other hand, these real-world patients were diagnosed with standardized assessment tools, enhancing diagnostic accuracy. The authors believe that this latter issue goes to the heart of the current controversy in youth bipolar disorder. In many settings, where diagnostic accuracy is less than desirable, numerous patients may be diagnosed with bipolar disorder without clearly meeting pre-established criteria. The explosion in bipolar disorder diagnoses in youth is probably in large part related to inadequate diagnostic workups. Emerging data show that it will be important to increase diagnostic precision, since, among other things, diagnosis predicts prognosis.[5] Researchers are starting to show that the longitudinal course, family history, and pathophysiology of bipolar disorder versus mood disorder NOS is quite different.[11,12] The present study also shows that it is important, in real-world settings, to differentiate both conditions: Patients with mood disorder NOS improved significantly less than patients with bipolar disorder, despite similar treatment intensity and pharmacotherapy.

In this clinic, bipolar disorder patients were significantly older. Both groups had comorbidity, although ADHD was much more common in mood disorder NOS patients, a finding that is also discussed in research studies.[13] These latter two observations, the age difference and the comorbidity difference, may be related: Mood disorder NOS patients are reported to have a high comorbidity with ADHD and oppositional defiant disorder, both of which have an earlier onset than bipolar disorder.[13]

Patients with bipolar disorder

appeared to have a more significant past histories, including more risk factors for suicidality, more medication trials, and more psychiatric hospitalizations. As such, they looked more like adults with bipolar disorder. Despite these factors, they improved much better under the current treatment conditions. One wonders if this finding is related to a better understanding of the treatment needs of bipolar patients compared to severely mood disordered patients. In this regard, upon reviewing the specific medications, it is of note that, at endpoint, there were significant differences in the pharmacotherapy of the two conditions: Many more patients with bipolar disorder were taking anticonvulsant mood stabilizers (42% versus 5%), while 14 percent of mood disorder NOS patients received no longer mood stabilization (0% in bipolar group).

One finding, contrary to research results, was the increased incidence of a family history of bipolar disorder in mood disorder NOS patients. This finding, however, is difficult to interpret without direct evaluation of the family members. Indeed, in real-world settings, not only youth but also adults may be overdiagnosed with bipolar disorder, as such inflating the reported family histories.

In summary, this study shows the feasibility of putting standardized assessment tools into place in a busy clinic setting. In doing so, guidelines for diagnosing youth with different mood problems can be followed. This has led to the identification of significant differences in the outcome between patients with bipolar disorder and mood disorder NOS.

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